D9965147 "C4E7C1

ACGAAGATGATGTTGAAGCTTATGTGGAATTTGTGAGATTCTGGATTAAAATTTGTGGCTCATAAAGCATTTCTGAAAAACAGCAACCTGCAGCACCTGCAGCACTTAAATTTTA E D D V E A Y V G L R N L T I V D S G L K F V A H K A F L K N S N L Q H I N F T CCTGGATAAGGTGGCATGGACCCGCCATGGCGCGCTTCTGCTGGTTGTGGGCTTCTGGAGGGCCGCTTTCGCCTGTCCCACGTCCTGCAAATGCAGTGCCTCTCGGA WIRWHGPAMAS CKCSASTGCCTCTCGG WIRWHGPAMAS CKCSASTCTCTGCTGGTTGTGGGCTTCTGGAGGGCCGCTTTCGCCTGTCCCACGTCCTGCAAATGCAGTGCCTCTCGGA TCTGGTGCAGCGACCCTTCTCCTGGCATTTCCGAGATTGGAGCCTAACAGTGTAGATCCTGAGAACATCACGGAAATTTTCATCGCAAACCAGAAAAGGTTAGAAATCATCA W C S D P S P G I V A F P R L E P N S V D P E N I T E I F I A N Q K R L E I I N CCCGAAACAAACTGACGAGTTTGTCTAGGAAACATTTCCGTCACCTTGACTTGTCTGATCCTGGGGGCAATCCATTTACATGCTCCTGTGACATTATGTGGATCAAGACTCTCC R CACCT<u>AACCTCACTG</u>TGGAGGAAAGGTTATCCATATCCTGTAGTGTGGCAGGTGATCCGGTTCCTAATATGTATTGGGATGTTGGTAACCTGGTTTCCAAACATATG<u>AATGAAA</u> P <mark>N L T V</mark> E E G K S I T L S C S V A G D P V P N M Y W D V G N L V S K H M N E T 1 GGAAGGTTTAAAGAAGCCGCAAAGGGCCTCCCGGCACGGGTGGGGGAAAGCGGCCGGTGCAGGGGGGGACAGGCACTCGGGCTGGCACTGGCTAGGGATGTCGT - 3.1 CAAGCCACACACAGGGCTCCTTAAGGATAACTAACATTTCATCGATGACAGTGGGAAGCAGATCTCTTGTGGGGGAAAATCTTGTAGGAGAAGATCAAGATTCTGTCAACCTCACTG TGCATTITGCACCAACTAICACATTICICGAATCICCAACCICAGACCACCACTGGTGCATTCATICATGTGAAAGGCAACCAAAACCAGGGGTTCAAAACGGGGCAAA H F A P T I T F L E S P T S D H H W C I P F T V K G N P K P A L Q W F Y N G A I TATT<u>GAATGAGTCCAA</u>ATACATCTGAAAATACATGTTACCAA<u>TCACACGG</u>AGTACCACGCTGCCTCCAGGTGAATAATCCCACTCACATGAAAAATAGAGGACTACACTCTAATAG L <mark>N E S K</mark>YIC T KIH V T N H T E Y H G C L Q L D N P T H M N N G D Y T L I A CCAAGAATGAGTATGGGAAGGATGAGAATTTCTGCTCACTTCATGGGCTGGCCTGGAATTGACGATGGTGCAAACCCAAATTATCTAAAAATTATGAAGATTATGGAACTG KNEYGKDEYGKDEKQISA HFMGWPGCTGGCTGGAATTGACGATGGTGCAAACCCAAATTATCTGAGAATTATGAAGATTATGGAACTG 121 841 241 13 361 53 481 961 253 601 133 1081 293 1201

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AGCTCAAGCCAGACACATTGTTCAGCACATCAAAACATTGTTCTGAAAAGGGAGCTAGGCGAAGGAGCCTTTGGAAAAGTGTTCCTAGCTGAATGCTATAACCTCTGTCCTG 2401 TAGAGTGTATCACTCCAGAGCCCACGACCCCCCACGAGGAGGTGTATGAGCTGATGCTGGGGGGCGCAGCGAGAGCCCCACATGAGGAAGAACATCAAGGGCA 733 E C I T Q G R V L Q R P R T C P Q E V Y E L M L G C W Q R E P H M R K N I K G I 1801 AGCAGGACAAGATCTTGGTGGCAGTGAAGAATGCAGTGACAATGCACGCAAGGACTTCCACCGTGAGGCCGAGCTCCTGACCAACCTCCAGCATGAGCACATCGTCAAGT 533 Q D K I L V A V K T L K D A S D N A R K D F H R E A E L L T N L Q H E H I V K F TCTATGGCGTCTGCGTGCAGGCCTCATCATGGTCTTTGAGTACATGAAGCATGGGGACCTCAAGAGTTCCTCAGGGCACACGGCCCTGATGCCGTGCTGATGGCTGAGGGCA ACCCGCCCACGGAACTGACGCAGATGCTCAGATGCCCAGCAGATGGCGTGCTTGGCGTCCCAGCACTTCGTGCGCGATTTGGCCACCAGGAACTGCC 2281 AGAGCATCATGTACAGGAAATTCACGACGACGAGGACGTCGGGGGTCGTGTTGGGGAGATTTTCACCTATGGCAAACAGCCCTGGTACCAGCTGTCAAACAATGAGGTGA 693 SIMYRKFTTE SDVWSLGVV SVVLWE'IFTYG KOPWYQLSNNEEVI 2521 TCCATACCTTCTTCAGAACTTGGCCAAGGCATCTCCGGTCTACCTGGACATTCTAGGCTAGGGCCCTTTTCCCCAGACGATCCTTCCCAACGTACTCCTCAGAGGGCTGAGAGGATG 2641 AACATCTTTTAACTGCCGCTGGAGGCCACCAAGCTGCTCTCCTTCACTCTAACATTAACATCAAAGACTCCGAGAAGCTCTCGAGGGAAGCAGTGTACTTCTTCATCCATAGACA 2881 TTACCCTTTCTTTGAATCAATCTGGCTTCTGCATTACTATTAACTCTGCATAGACAAAGGCCTTAACAAACGTAATTTGTTATCAGCAGACACTCCAGTTTGCCCACCACAACTAAC 2161 653

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1631 GTTGGCTTATCCCGGGAAGTGCTGCTTATCTGGGTATTTCTGGTAGATGTGGGCGGTGTTTGGAGGCTGTATATGAAGCCTGCATATACTGTGAGCTGTGATTGGGGAACACCAATG 1751 CAGAGGTAACTCTCAGGCAGCTAAGCACCTCAAGAAAAACATGTTAAATTCTTCTTTTACAGTAGTTCAAATACAAAACTGAAATGAAATCCCATTGGATTGTACTTCTCT

FIG. 10

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- 241 ATCTCAAGGAATATCACTTCCATACACATGAGAACTGGGGGGTCTCAACGCGGTGGACGTGGAGCTCTACACGGACTTCAAAAGCTGACCATCAAGAACTCAGGACTT 45 I S R <mark>N I T S</mark> I H I E N W R S L H T L N A V D H E L Y T G L Q K L T I K N S G L
- CGGAGCATTCAGCCCAGAGCCTTTGCCAAGAACCCCCATTTGCGTTATATAAACCTTCAGAGTAACGGCTCACCACACTCTCGTGGCAGCTCTTCCAGACGCTCAGACTTCGGGAATTG Z 361
- CAGTTGGAGCAGAACTTTTTCAACTGCAGCTGTGACATGCAGCAGCAGGAGGAGGCCAAGCTCAACAGCTCTACTGCATCAATGCTGATGGCTCA Q L E Q N F F N C S C D I R W M Q L W Q E Q G E A K L N S Q N L Y C I N A D G S
- CAGCTICCICTICCGCATGAACATCAGTGAGACCTTCCTGAGATCAGCGAGCCACGTGACCGTACGAGGGGGGACAATGCTGTATCACTTGCAATGGCTCTGGA Q L P L F R M <u>N I S Q</u> C D L P E I S V S H V <u>N L T V</u> R E G D N A V I T C <u>N G S G</u>
- 721 TCACCCCTTCCTGATGTGGATAGTCACTGGGCTGCAGCCATCACAGACCAATCTGAACTGGACCAATGTTCATGCCATCAACTTGAGGCTGGAATGTGAGGAGT 205 S P L P D V D W I V T G L Q S I N T H Q T N L <mark>N W T N</mark> V H A I <mark>N L T L</mark> V N V T S
- 841 CAGCACAATGGCTTCACCCTGACGTGCATTGCTGGTGGCATGAGCAATGCCAGTGTTGCCCTCACTTACTATCCCCCACGTGTGGTGAGCCTGAGAGCCTGAGCTG 245 E D N G F T L T C I A E N V V G M S <mark>N A S V</mark> A L T V Y Y P P R V V S L E E P E L
- COCCTOGAGCACTOCATCGAGTTTGTGGGGGGAACCCCCCACCACGCTGCACTGGCTGCAATGGGCAGCCTCTGGGGAGTCCAAGATCATCCATGTGGAATACTACCAAGAG R L E H C I E F V V R G N P P P T L H W L H N G Q P L R E S K I I H V E Y Y Q E
- GGAGAGATTICCGAGGCTGCTGCTTCAACAAGCCCACCACTACAAACCCTGATTGCCTAAAAACCCACTGGGCACAGCCAACCAGACCATCAATGGCCACTTC
- 1201 CICAAGGAGCCCTITICCAGAGACTITIAICTITICACGAAGTGAGTCCCACACCTCTAICACTGTGACCCACAACCAGAAGAAGACACTITIGGGGTAICCATAGCA $365\,\mathrm{L}$ K E P F F F E D T E G V S I A $365\,\mathrm{L}$ K E P F F E D T E G V S I A
- 1321 GTTGGACTTTGCTGCTGTTGCTGTTGGTGTTCTTTCGTCATGATCAACAAATATGGTCGACGGTCCAAATTTGGAATGAAGGGTCCCGTGGCTGTCATCAGTGGTGAGGA O S > 4 > a U E E × S œ œ U 405 Y G L A A F A C Y L L V Y L F V M I N R Y
- 1441 GACTCAGCCAGCCACCACCACACACACACGCCACACGCCCTCGTCACTGGATGCCGGGCCCGACACTGTGGTCATTGGCATGCCATCCCTGTCATTGAGAACCCCAG 445 D S A S P L H H I N H G I T T P S S L D A G P D T V V I G M T R I P V T E N P A

FIG. 2A

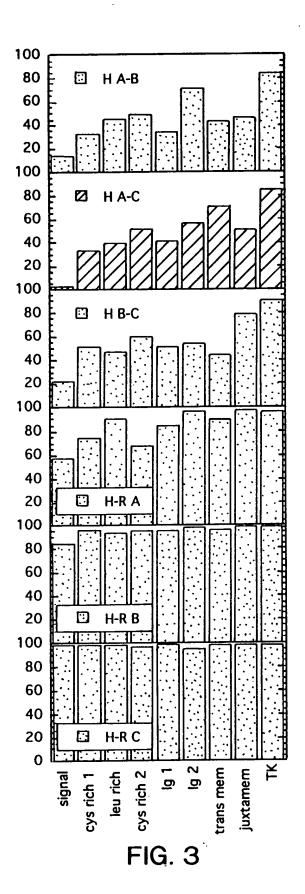
2041 GTGCACCGAGACCTGGCCACGGAACTGCTGGAATCTGCTAGTGAGATTGGGGACTTCGGCATGTCCAGAGATGTCTACAGCACGGATTATACAGGCTCTTTAATCCA 645 V H R D L A T R N C L V G A N L L V K I G D F G M S R D V Y S T D Y Y R {L F N P CCCAAAGAGGTGTACGATGCTGGGGTGCTGGCAGGGGACCACGGGTTGAACATCAAGGAGATCTACAAAATCCTCCATGCTTTGGGGAAGGCCACCCCAATCTACCTG ${}^{
m P}$ ${}^{$ CAGCATGAGCACATTICTACAGTTCTATGAGTGTGGGGACCCCTCATCATGGTCTTTGAATACATGAGCATGGAGCCTGAATAAGTTCCTCAGGGCCCATGGGCCAAAA Q H E H I V K F Y G V C G D G D P L I M V F E Y M K H G D L N K F L R A H G P D 2161 TCTGGAAATGATTTTTGTATATGGTGGGGGGGGGGGGCACCATGCTCCCTGGATGCCTCCTGAAAGCATCATGTACGGAAGTTCACTACAGAGGGAAGTGATGTATGGAGC685~S G $_{
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FIG. 2B

1720 TACCCAAGGTCACATGGTTTCAGAAATTATGTTGAATCCAATAAGCCTTCCCGGACATTCCAAGCCTCTTAACCATGGCATGTTGAGGAAGGTAATTTTCAGCAAAGGA 538 Y P R S H G F R E I M L N P I S L P G H S K P L N H G I Y V E D V N V Y F S K G

1840 CGTCATGGCTTTTAAAAAC 578 R H G F O

FIG. 2C



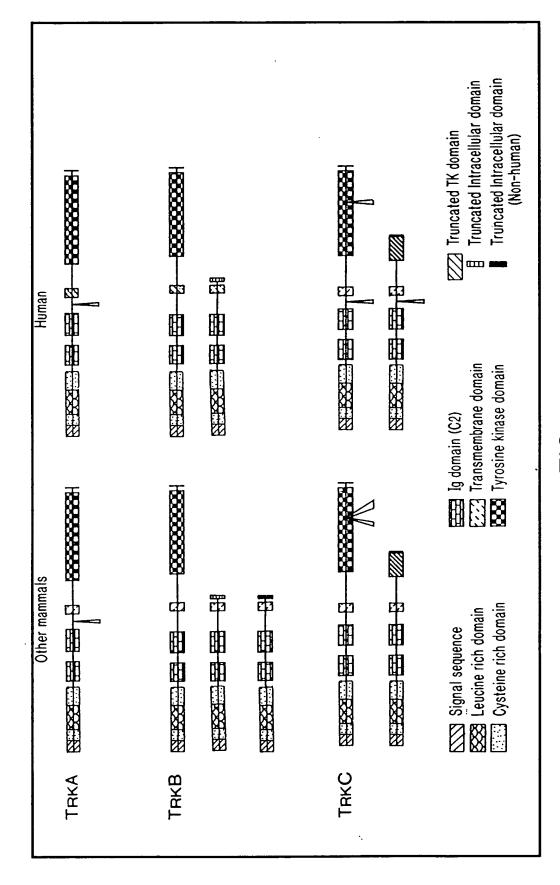


FIG. 4

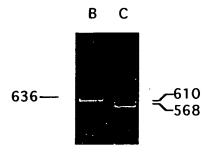


FIG. 5

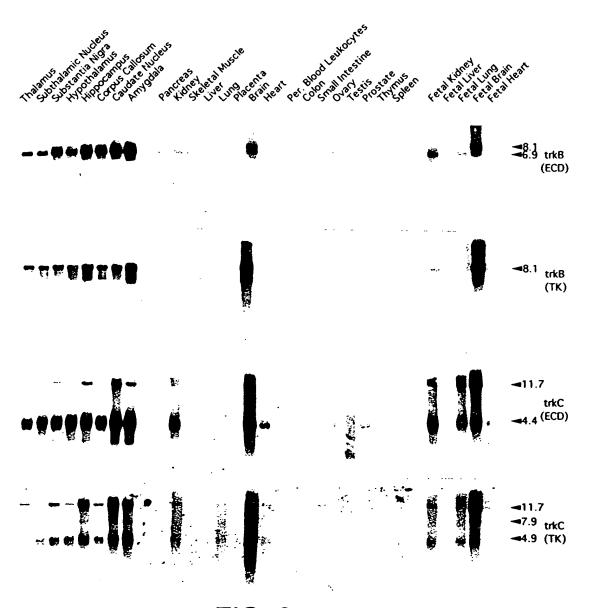
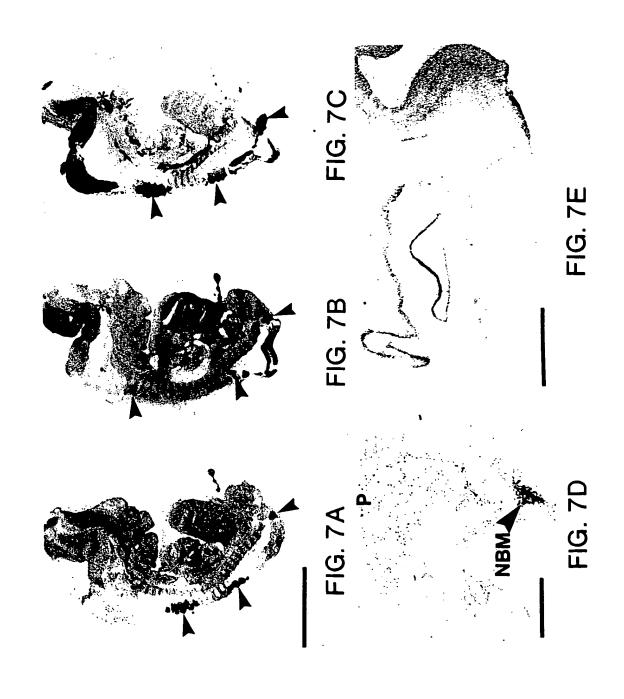
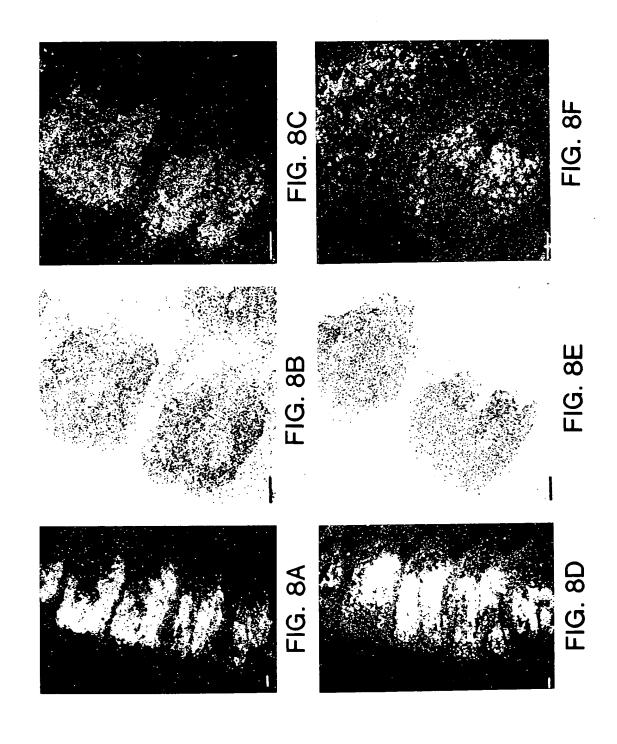
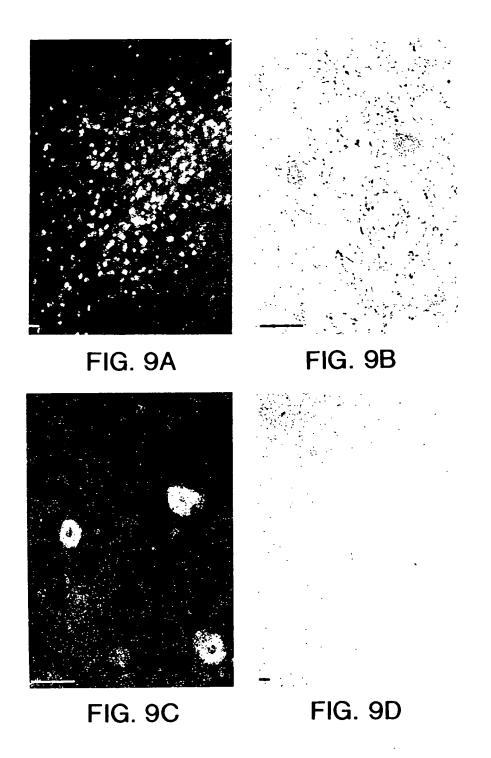


FIG. 6







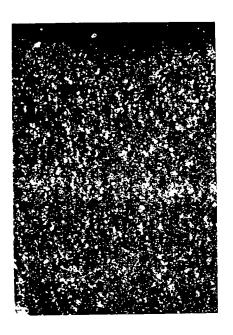


FIG. 9E

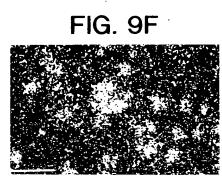
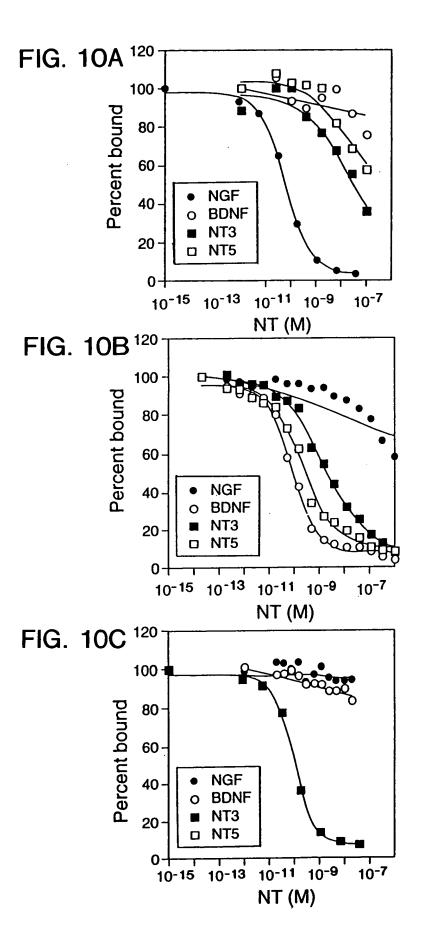
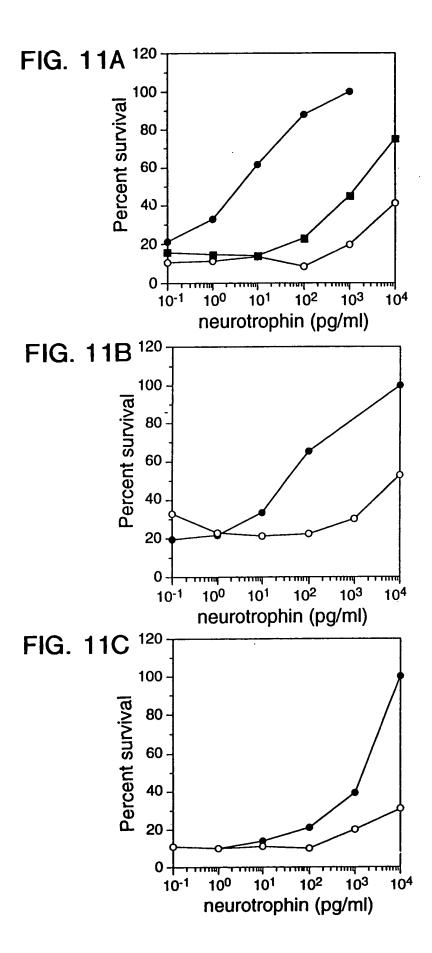


FIG. 9G





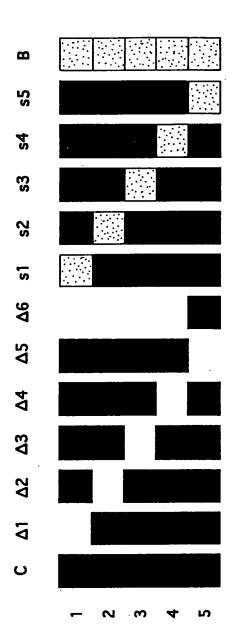
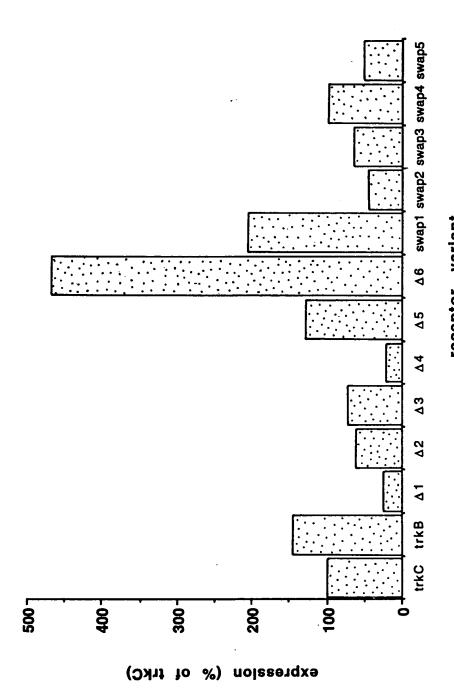
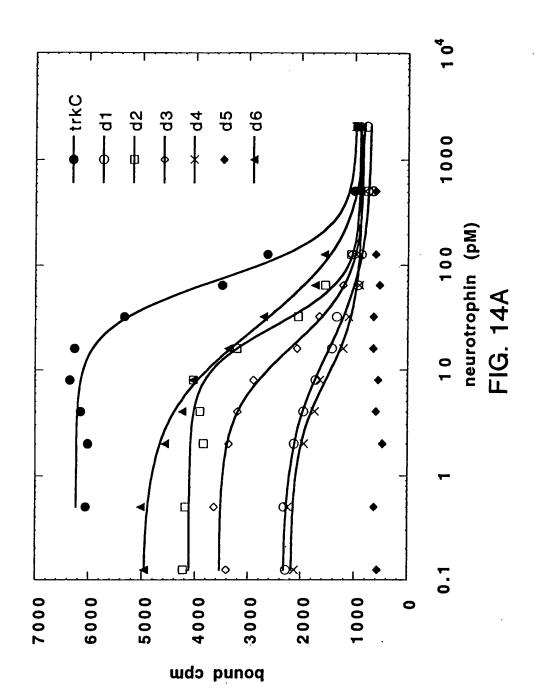
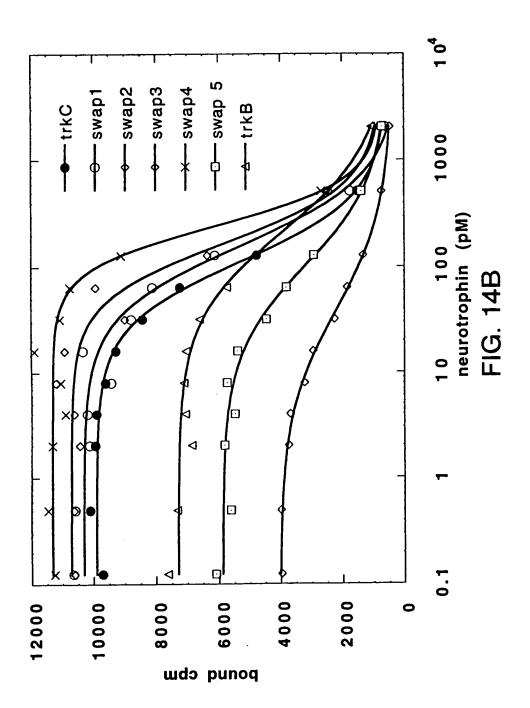


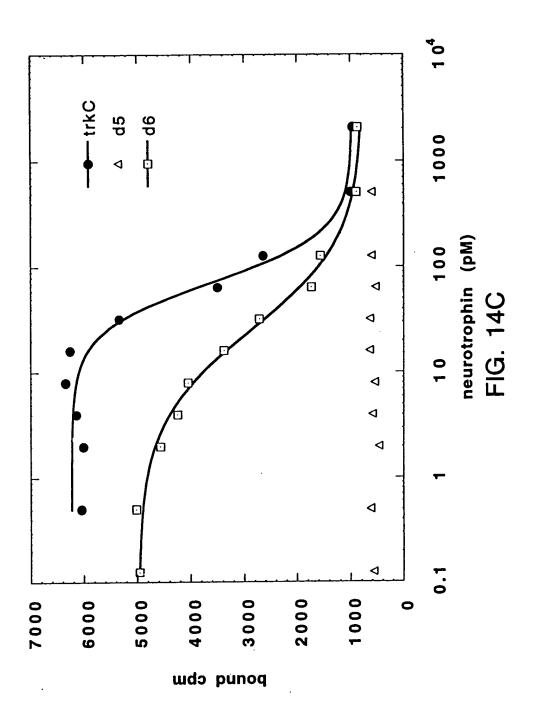
FIG. 12

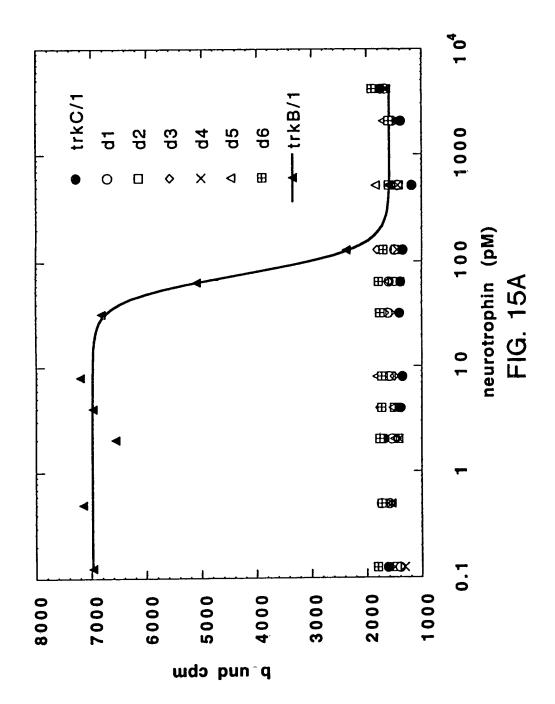


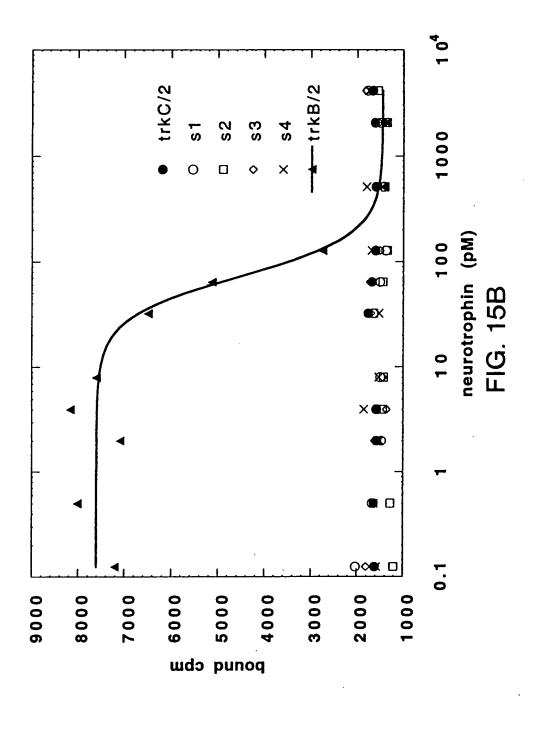
receptor variant FIG. 13

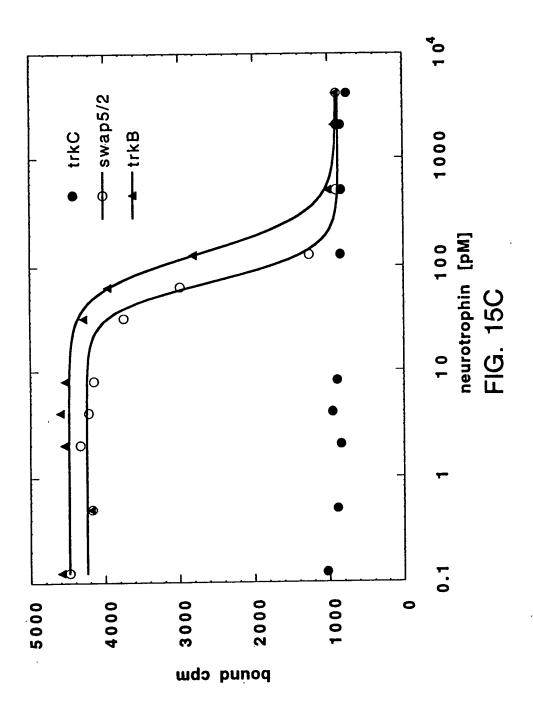












M S S W I R W H G P A M A R L W G F C W L L V V G F W R A A F A C P T S M D V S L C P A K C S F W R I - F L L G S V W L D Y V G S V L A C P A N S S G L R C T R - D G A L D S L H H L P G A E N L A S R I W C S D P S P G I V A F P R L E P N S V D P E N I K I E I N C R P D D G N L - F P L L E G D D S G N S N G N A N I N I T D I S R N I O H L E L R D L R G L G E L R N L T I V K S G L R F V A P D A F H F T P R L S R L N E I I N E D D V E A Y V G L R N L T I V K S G L R F V A P D A F H F T P R L S R L N H T L N A V D M E L Y T G L D K L T I I K N S G L R F V A H K A F L K N S N L D H I N Y I N L E S L S M K T V O G L S L D E L V L S G N P L H C S C A L R M L D R P G G E A O G P L A H M P N A S C G V P T L K V O V P N A S V D V G D D V L L R C O V E S S K N I P L A N L D I P R C G L P S A N L A A P N L T V R E G D N A V I T C N G E S S K N I P L A N L D I P R C G L P S A N L A A P N L T V R E G D N A V I T C N G E D A G M I L T E L E D S A T V M K S G G L P S L G I T L A N V T S D D S G K P P D V D W I V T G L O S I N T H O T N L N W I N V H A I N L T L V N V T S E D N G F	-	L =	7	2	ی	œ	1	0	_	5	I	2	3	X	S A	<u>ق</u> ۾	Ignal	<u> </u>		1		l .	-	~	∢			:	1:	١.	∢	၂ ပ	1) -	1		1	٦	۱ ۾					
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FIG. 16A

0 × -و حر <u>ی</u> KFG GDYTLIAKNE × N A A NYTLIAKN S S **w w w** _ _ _ w z **ex ex** 3 3 3 7 1 L L > S G R E H L S V Y A V V V I A S V V G F - C - L L V M L F L L - - K L A E E D - - - T F G V S I A V G L A A F A C V L L V V L F V M I N K Y G ၒ **=** • ۵ х С Z S N L Q œ GIDDGANPNYPDVIYEDYGTAANDIGDTT GVSVAVGLAVFACLFLSTLLLVLN × ۵. X. z Z z 9 1 7 E V S DAVIIG DPIP ပ N > GAILNESKYICTKIH - - VINHTEYHGCLOLDNPTHMN GOPLRESKIIHVEYY - - OEGEIS - EGCLLFNKPTHYN 0 1 0 ပ ပ ပ V G R A E V S V O V N V S F P A S V O - L H T A V E M H H W C 1 P F S V D V G E D O D S V N L T V H F A P T 1 T F L E S P T S D H H W C 1 P F T V K V G M S N A S V A L T V Y Y P P R V V S L E E P E L R L E H C 1 E F V V R > 1 d 0 10 w PFPEST-DNF-ILF — Transmembrane — Juxtamembrane LSPIE-GKGS ۵. ۵. ۵ z . E F . N SEGGILDAGI ب œ ر ر S S • ပ S ٠ S × 6 S S L S R T P S ETVR • • 4 ပ ပပ M T L Z. z w I S Z <u>0</u> . . × DGLAMSLHFMT DDSASPLHHIS :DSASPLHHIN • ٠ ٩ 7 3 0 ۵. ٠ • 3 OISAHFMG - TSGDPVEKK IPSTDVTDKT DVIDKI Ω **6** w £ ANOTINGHFL ۵. G P A S V I S N D D G P V A V I S G <u>E</u> E AAF × ۵ 1 1 1 SVLN ∢ N I N > ∢. A S A D E K ۵. œ 272 290 370 466 448 99 387 新芳 新秀 新育 Ş

FIG. 16B

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E L G

DIYVOHIKRRDIVLKR

SOLKP

z

NPOYFGIT

z

NCHKP

<u>ა</u>

OYFR

S

D A C V H H I K R R D I V L K W E L G E G A F G K V F L A E C H N L L P E D T F V O H I K R H N I V L K R E L G E G A F G K V F L A E C Y N L C P E

HIAGOIAL W I L W OIO م م م R P R A C P P E V Y A I M R G C W O R E P R P R T C P O E V Y E L M L G C W O R E P R P R V C P K E V Y D V M L G C W O R E P **ex ex ex** ~ ~ ~ GEDV-APGPLGLGOLLGNPP---TELTOSOMLGOPROAKGELGLSOML ပ ပ DIYSTDYY R D V Y S T D Y Y R D V Y S T D Y Y G ပ S S 3 3 3 > > > 0 SSS SSS **x x x** ပ ပ ပ R N C L V G O G L V V K I G D F R N C L V G E N L L V K I G D F R N C L V G A N L L V K I G D F **ac ac ac** w I x 0 0 2 Z LLMVFEYMRHGDLNRFLRSHGPDAKLLAG LIMVFEYMKHGDLNKFLRAHGPDAVLMAE LIMVFEYMKHGDLNKFLRAHGPDAMILVD w w w م م a a a * **E** E Y G K O P W Y O L S N T E A I D C I T O G R E L E Y G K O P W Y O L S N N E V I E C I T O G R V L O Y G K O P W F O L S N T E V I E C I T O G R V L E ∢ ∢ 0 F O R E A D F O R E A D F O R E A 6 R H T H D \times **a**c ac ac G M V Y L A S O H F V H R D L A T G M V Y L A S O H F V H R D L A T RDLAT D X A A G ပ ပ **>** · · · S S GLHFVH KILVAVKTLKDA ٩ **a** • • • • • • • KMLVAVKALK Tyrosine Kinase – 14 • Ω z GMVYLA ပ ؎ z 749 266 788 266 663 988 717 532 \$ \$ \$ \$ 新春春 話を

FIG. 16C

0 0 0

PIYLDIL

NIKEIYKILHALGKAT

R H S I K D V H A R L O A L A O A P P V Y L D V L R K N I K G I H T L L O N L A K A S P V Y L D I L

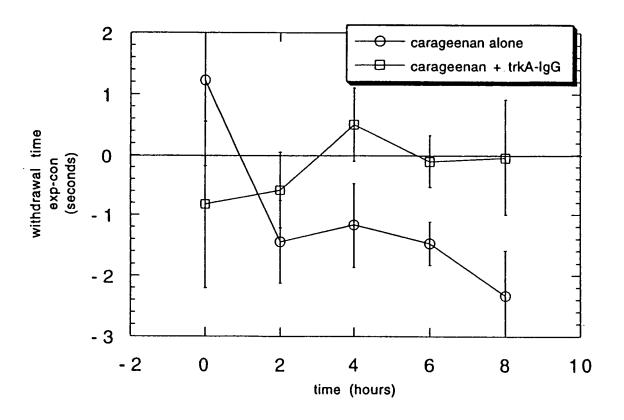


FIG. 17

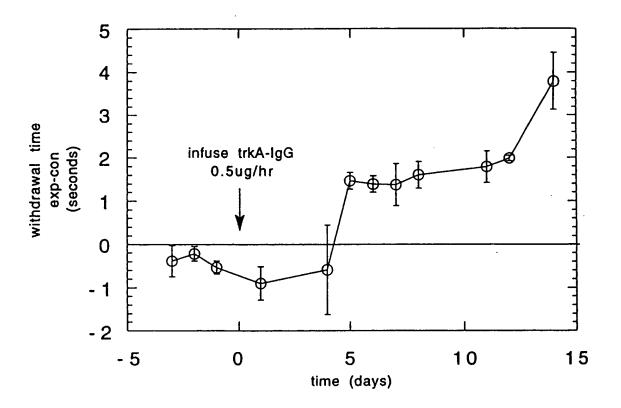


FIG. 18